

REC'D 22 FEB 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

4

Applicant's or agent's file reference 12/199-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/07832	International filing date (day/month/year) 15/10/1999	Priority date (day/month/year) 16/10/1998
International Patent Classification (IPC) or national classification and IPC C12N15/12		
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 19/04/2000	Date of completion of this report 19.02.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Fotaki, M Telephone No. +49 89 2399 8709



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/07832

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).*):

Description, pages:

1-34 as originally filed

Claims, No.:

1-14 as originally filed

Drawings, sheets:

1/11-11/11 as originally filed

Sequence listing part of the description, pages:

1-18, as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/07832

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:
see separate sheet

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

- ☐ copy of the earlier application whose priority has been claimed.
- ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1, 2, 4-11
	No:	Claims 3, 12-14
Inventive step (IS)	Yes:	Claims 1, 2, 4-11
	No:	Claims 3, 12-14
Industrial applicability (IA)	Yes:	Claims 1-14
	No:	Claims

2. Citations and explanations
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/07832

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/07832

I. BASIS OF THE REPORT

- 1) Sequence listing pages 1/18-18/18 are also included in the basis of the report.

II. PRIORITY

- 2) This first preliminary written opinion has been established after consideration of the priority document EP 98 119 583.7 of 16.10.98. Therefore, documents
*AARNOUDSE, C. A. ET AL.: 'Interleukin-2-induced, melanoma-specific T cells recognize CAMEL, an unexpected translation product of LAGE-1.'
INTERNATIONAL JOURNAL OF CANCER, vol. 82, no. 3, 30 July 1999, pages 442-8;
*WO 99 18206 A , 15 April 1999;
cited in the international search report are not relevant in establishing the novelty of the present invention.

V. REASONED STATEMENT UNDER RULE 66.2 (a) (ii)

- 3) Reference is made to the following documents:
D1: WANG, R.-F. ET AL.: 'A breast and melanoma-shared tumor antigen: T cell responses to antigenic peptides translated from different open reading frames.'
JOURNAL OF IMMUNOLOGY, vol. 161, 1 October 1998 (1998-10-01), pages 3596-606;
D2: WO 98 32855 A (GODELAINE DANIELE ;LETHE BERNARD (BE); LUCAS SOPHIE (BE); SMET CHA) 30 July 1998 (1998-07-30)
- 4) The present application relates to the identification of a cDNA clone (4H8) with nucleotide sequence SEQ ID NO 1 which encodes a tumor associated antigen, called CAMEL, with amino acid sequence SEQ ID NO 2. Said polypeptide represents an alternative ORF of the known gene sequence NY-ESO-1 (document D1, ORF1/ORF2) or LAGE-1 (document D2, splice variants SEQ ID NO's 5, 7, 9). The novel polypeptide is shown to contain at least one antigenic epitope inducing recognition by melanoma specific cytotoxic T lymphocytes (CTL). Many of the tested breast and lung cancer tissue specimens comprise the corresponding mRNA and express CAMEL polypeptide (monitored by CAMEL-

specific antiserum). Five polypeptides (SEQ ID NO 11, 12, 24, 25, 26) were shown to be immunogenic, inducing a CTL response by being presented by HLA molecules.

The closest prior art document D1 presents, on Figure 3, a putative ORF of the disclosed gene NY-ESO-1, ORF2. Said ORF is identical to the CAMEL polypeptide over a region of residues 1-53 out of the entire length of 109 amino acids. The prior art document does not disclose nor enables the provision of the CAMEL polypeptide with SEQ ID NO 2. Furthermore, said document discloses immunogenic polypeptides derived from putative ORF2 (Figure 3 and page 3601) which however, are not the same as the one identified in the present application. Document D2 discloses three putative ORFs of the LAGE-1 gene sequence resulting from alternative splicing, none of which is compatible with the CAMEL polypeptide.

Therefore, in light of the cited prior art documents, the subject-matter of the present application as claimed in **Claims 1, 2, 4-11** is novel and inventive.

- 5) The subject-matter of **Claim 3** is not novel as required by Article 33(2) PCT.

Said claim relates to immunogenic (poly)peptide derived from the CAMEL polypeptide. The subject-matter of said claim is only defined by the functional feature "immunogenic" which renders the subject-matter so vague as to cover any immunogenic epitope, also known ones, which happened to have sequence encompassed in SEQ ID NO 2.

- 6) The subject-matter of **Claims 12-14** is not novel as required by Article 33(2) PCT.

Said claims relate to a DNA molecule comprising the sequence of SEQ ID NO:1. Document D2 discloses the sequence of gene LAGE-1 which is such a DNA molecule as shown in Figure 2A of the present application. The use of said molecule in cancer therapy is also disclosed in said document (p. 9).

VI. CERTAIN DOCUMENTS CITED

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP99/07832

- 7) The following documents are cited under Rule 70.10 PCT

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 99 18206	15.04.99	21.09.98	08.10.97

VIII. CERTAIN OBSERVATIONS ON THE INTERNATIONAL APPLICATION

- 8) The Applicant is reminded that the claims must be comprehensible from the technical point of view and clearly define the object of the invention, that is to say indicate all the essential features thereof (Rule 6 PCT). The subject-matter of **Claim 3** does not fulfil this condition, as the claimed nucleic acid is only defined by a functional feature without disclosing any technical feature which unambiguously characterizes the claimed subject-matter. A polypeptide being a chemical product should be clearly defined by its formula i.e. its amino acid sequence.

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 12/199-PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.	
International application No. PCT/EP 99/ 07832	International filing date (day/month/year) 15/10/1999	(Earliest) Priority Date (day/month/year) 16/10/1998
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the International search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.

☐ the International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, the International search was carried out on the basis of the sequence listing :

☒ contained in the International application in written form.

☒ filed together with the International application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

CAMEL, AN ALTERNATIVE TRANSLATION PRODUCT OF THE TUMOUR ANTIGEN LAGE-1

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☒ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

2a _____

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

P 99/07832

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WANG, R.-F. ET AL.: "A breast and melanoma-shared tumor antigen: T cell responses to antigenic peptides translated from different open reading frames." JOURNAL OF IMMUNOLOGY, vol. 161, 1 October 1998 (1998-10-01), pages 3596-606, XP002096029 the whole document	12-14
X	WO 98 32855 A (GODELAINE DANIELE ; LETHE BERNARD (BE); LUCAS SOPHIE (BE); SMET CHA) 30 July 1998 (1998-07-30) see whole document, particularly the claims	12-14
	--- -/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

17 March 2000

Date of mailing of the international search report

24/03/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Smalt, R

INTERNATIONAL SEARCH REPORT

International Application No

P 99/07832

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>VAN ELSAS, A. ET AL.: "Transfection of IL-2 augments CTL response to human melanoma cells in vitro: immunological characterization of a melanoma vaccine." JOURNAL OF IMMUNOTHERAPY, vol. 20, no. 5, September 1997 (1997-09), pages 343-53, XP002096030 cited in the application abstract; figures 6B,7</p>	
P,X	<p>AARNOUDSE, C. A. ET AL.: "Interleukin-2-induced, melanoma-specific T cells recognize CAMEL, an unexpected translation product of LAGE-1." INTERNATIONAL JOURNAL OF CANCER, vol. 82, no. 3, 30 July 1999 (1999-07-30), pages 442-8, XP000867744 the whole document</p>	1-4,9-14
P,X	<p>WO 99 18206 A (WANG RONG FU ;GOVERNMENT OF THE UNITED STATE (US); ROSENBERG STEVE) 15 April 1999 (1999-04-15) claims 24,26,27,37; figures 3A,7A</p>	3,9,11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PO 99/07832

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9832855	A	30-07-1998	US	5811519 A	22-09-1998
			AU	6042198 A	18-08-1998
			EP	0970206 A	12-01-2000
			ZA	9800656 A	17-08-1998
<hr/>					
WO 9918206	A	15-04-1999	AU	9572098 A	27-04-1999
<hr/>					